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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,287	10/03/2001	Maria Alexandra Glucksmann	10147-61U1 (MPI2000-471PI)	9083

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Intellectual Property Group
MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/970,287

Applicant(s)

GLUCKSMANN ET AL.

Examiner

Terra C. Gibbs

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2004 and 24 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-37, 39-45 and 47-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-37, 39-45 and 47-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This Office Action is a response to Applicants Amendment and Remarks filed April 1, 2004 and May 24, 2004.

In the Amendment filed April 1, 2004, claims 1-30 were canceled and new claims 31-46 were added. In the Amendment filed May 24, 2004, claims 38 and 46 were canceled and new claims 47-49 were added.

Claims 31-37, 39-45, and 47-49 are pending in the instant application. Claims 31, 36, 39, and 44 have been amended.

Claims 31-37, 39-45, and 47-49 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Change in Power of Attorney

Applicant's change in Power of Attorney, filed April 1, 2004 is acknowledged.

Oath/Declaration

Applicants have submitted a declaration under 37 CFR §10.9(b), filed April 1, 2004 and May 24, 2004. The declarations filed April 1, 2004 and May 24, 2004 are duplicates. The declaration under 37 CFR §10.9(b), filed May 24, 2004 is acknowledged by the Examiner.

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Response to Remarks

Applicants Amendment and Remarks filed April 1, 2004 and May 24, 2004 addresses the previous Office Action, mailed November 18, 2003. In the previous Office Action mailed November 18, 2003, claims 1-30 were examined. Applicants have subsequently canceled claims 1-30 and added new claims 31-37, 39-45, and 47-49. **Therefore, Applicants Remarks filed April 1, 2004 and May 24, 2004 are moot.**

Applicant's amendment necessitated the new ground(s) of rejection presented below:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-37 and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO: 1 and 3 which correspond to the cDNA and genomic DNA, respectively, encoding the human species of 22437 protein, SEQ ID NO:2. Claims 31-37 and 47-49 are directed to encompass methods comprising a polypeptide which is at least 95% identical to SEQ ID NO:2, or a polypeptide fragment comprising 400 amino acid

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residues of SEQ ID NO:2, which exhibit sulfatase activity. The issue is would a polypeptide which is at least 95% identical to SEQ ID NO:2, or a polypeptide fragment comprising 400 amino acid residues of SEQ ID NO:2 as recited in claim 31, exhibit sulfatase activity as claimed? The specification does not teach any polypeptides which are at least 95% identical to SEQ ID NO:2 that retain the function of exhibiting sulfatase activity. Similarly, the specification does not teach a polypeptide fragment comprising 400 amino acid residues of SEQ ID NO:2, which exhibits sulfatase activity. The specification provides insufficient written description to support the very broad genus of polypeptides and fragments of polypeptides used in the methods encompassed by the claims.

While it is known that many amino acid changes and substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid changes and substitutions can be tolerated such that functionality is retained are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions where the biological activity resides or regions directly involved in binding, stability, or catalysis; and in providing the correct three-dimensional spatial orientation for biologically active or binding sites, or for sites which represent other characteristics/properties of the protein. These or other regions may also be critical determinants of antigenicity of the protein of interest. These regions can tolerate only relatively conservative changes or substitutions or no changes or substitutions (see Bowie et al., 1990. Science, Vol. 247, pp. 1306-1310, especially p. 1306, column 2, paragraph 2; and see Ngo et al., The Protein Folding Problem and Tertiary Structure Prediction). Applicants have provided no guidance in

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this regard and the functionality recited in the claims is not considered by itself to elucidate what structure the polypeptides of the claimed methods would possess.

Applicant is referred to the Guidelines on Written Description, published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The central issue of this rejection is whether Applicant has described a sufficient number of species to adequately represent the genus of polypeptides of the claimed methods which are at least 95% identical to SEQ ID NO:2, or polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity.

The specification does not teach any polypeptides which are at least 95% identical to SEQ ID NO:2, or any polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibits sulfatase activity. In view of Applicants lack to disclose any species of the polypeptides of the claimed methods, and the failure to provide the structure of polypeptides which are at least 95% identical to SEQ ID NO:2, or polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity, one of skill in the art

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would conclude that Applicant was not in possession of the claimed invention at the time of filing, since functionality alone as recited in the instant claims to identify the polypeptides of the claimed method does not elucidate the structure (e.g. amino acid sequence) of the polypeptide having such function.

Response to Arguments

It is noted that in the previous Office Action mailed November 18, 2003, claims 28-30 were rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. It is noted that the Amendment filed April 1, 2004, canceled claims 28-30. However, in light of the presenting pending claims, the Examiner will address Applicants arguments. Applicants argue that they were in possession of the claimed invention at the time of filing. Applicants argue that the specification teaches that biologically active polypeptide fragments used in the claimed invention may include sequences of at least 400 contiguous amino acids of SEQ ID NO:2. Applicants point the Examiner to page 19. Applicants further argue that the specification teaches that isolated polypeptide molecules used in the invention include polypeptide sequences which are at least 95%, or more homologous to the entire length of the polypeptide sequence shown in SEQ ID NO:2. Applicants point the Examiner to page 33. Applicants argue that the specification teaches domains within the sulfatase polypeptide which are conserved and essential for activity of the polypeptide, namely the transmembrane domain and the sulfatase domain. Applicants point the Examiner to page 9. Applicants argue that the specification also teaches which regions of the polypeptide are amenable to alterations as well as those which are not amenable to alterations. Applicants point the Examiner to pages 2-4.

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Applicants contend that an example of a specific fragment comprising 429 contiguous amino acids of SEQ ID NO:2 which exhibits the sulfatase activity, namely the sulfatase family domain located at about residues 44-472 of SEQ ID NO:2 is taught at page 9. Applicants also argue that the specification teaches how to generate function variants by performing conservative substitutions within the polypeptide used in the claimed invention. Applicants also argue that the specification provides one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired sulfatase activity.

Applicant's arguments have been fully considered, but are not found persuasive. Applicants specification at page 33, second full paragraph, recites, "in one embodiment the protein includes an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to SEQ ID NO:2". Applicant's specification, at page 19, last paragraph, recites, "A biologically active portion of a 22437 protein can be a polypeptide that for example, 10, 25, 50, 100, 200, 300, 400, 500, 600, 700, or 800 or more amino acids in length". These statements are very generic and provide no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to amino acid changes and substitutions and the nature and extent of changes that can be made in these positions in order to obtain protein that exhibits the functionality of the claims. Applicant's specification at page 9, lines 2-4 recites, "amino acid residues that are conserved among the polypeptides of the present invention, e.g. those present in the sulfatase domain are predicted to be particularly non-amenable to alteration". However, this statement is not a requirement of the claims and therefore, the skilled artisan is left to guess which alterations will devise a peptide of the claimed methods which is at least 95% identical to SEQ ID NO:2, or a polypeptide

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comprising a fragment of at least 400 contiguous amino acids of SEQ ID NO:2, which exhibit sulfatase activity. Furthermore, even if the above statement was a limitation of the claims, the predicted sulfatase domain (e.g. residues 44-472 of SEQ ID NO:2) has not been characterized as actually having sulfatase activity, except to speculate, since this **predicted** region exhibits homology with other potential sulfatase proteins. Applicant's specification, at page 9, second full paragraph, discloses a specific fragment comprising 429 contiguous amino acids of SEQ ID NO:2 (e.g. residues 44-472 of SEQ ID NO:2) which has sulfatase activity. The specification contemplates that residues 44-472 of SEQ ID NO:2 exhibit sulfatase activity based merely on the fact that this **predicted** region exhibits homology with other potential sulfatase proteins. The specification has given no guidance on the actual activity of residues 44-472 of SEQ ID NO:2, except to speculate that this region has sulfatase activity based on sequence homology with other proteins. Simple determination of sequence similarity would not predictably translate into a protein exhibiting biological activity as discussed by Bowie et al. and Ngo et al. above. Applicants argue that the specification teaches how to generate function variants by performing conservative substitutions within the polypeptide used in the claimed invention, however, as discussed above, it is known that many amino acid changes and substitutions are generally possible in any given protein, however, the positions within the protein's sequence where such amino acid changes and substitutions can be tolerated such that functionality is retained are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions where the biological activity resides or regions directly involved in binding, stability, or catalysis; and in providing the correct three-dimensional spatial orientation for biologically active or binding sites, or for sites which represent other

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characteristics/properties of the protein. These regions can tolerate only relatively conservative changes or substitutions or no changes or substitutions. Applicants have provided no guidance in this regard, and the functionality recited in the claims is not considered by itself to elucidate what structure the polypeptides of the claimed methods would possess. Applicants also argue that the specification provides one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired sulfatase activity, however, this is not found persuasive because the issue is whether Applicants have described the polypeptides of the claimed methods, in such full and concise terms to enable any person skilled in the art to make and use the invention. Applicants have not disclosed any species of polypeptides of the claimed methods which are at least 95% identical to SEQ ID NO:2, or polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity. Further, Applicants have failed to provide the structure of polypeptides of the claimed methods which are at least 95% identical to SEQ ID NO:2, or polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity. The functionality recited in the claims is not considered by itself to elucidate what structure the polypeptides of the claimed methods would possess and one of skill in the art would conclude that Applicant was not in possession of the claimed invention at the time of filing.

Claims 31-37, 39-45, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention, and the quantity of experimentation necessary.

Claims 31-37 and 47-49 are drawn to a method for identifying a candidate compound for modulating a proliferative disorder, comprising combining a compound with a sample comprising a polypeptide which is at least 95% identical to SEQ ID NO:2, wherein the polypeptide exhibits sulfatase activity; and a polypeptide comprising a fragment of at least 400 contiguous amino acids of SEQ ID NO:2, wherein the polypeptide exhibits sulfatase activity, under conditions suitable for binding, and assessing and selecting the compound capable of binding to the polypeptide. Claims 39-45 are drawn to a method for identifying a candidate compound for modulating a proliferative disorder, comprising combining a compound with a sample comprising a polypeptide of SEQ ID NO:2, under conditions suitable for binding, and assessing and selecting the compound capable of binding to the polypeptide.

As per the section 112, first paragraph, for lack of written description rejection (see page 3 above), applicants are not in possession of any polypeptides of the claimed methods which are at least 95% identical to SEQ ID NO:2, or any polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity. The specification provides insufficient written description to support the broad genus of polypeptides and fragments of polypeptides used in the methods encompassed by the claims. Because functionality alone as recited in the instant claims to identify the polypeptides of the claimed method does not elucidate

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the structure (e.g. amino acid sequence) of the polypeptide having such function, it would require undue experimentation to practice the invention as claimed. The quantity of experimentation required to practice the invention as claimed would involve the designing of polypeptides of the claimed methods which are at least 95% identical to SEQ ID NO:2, or polypeptide fragments comprising 400 amino acid residues of SEQ ID NO:2, which exhibit sulfatase activity. Without such specific guidance from the specification, the skilled artisan is left to guess what peptides possess such activity.

Further, the claims encompass methods wherein binding of generally any type of compound is tested for binding to a broad range of highly variant polypeptides, a major portion of which have not been described, and, therefore, also not characterized by the instant specification. As claimed, these methods are intended to identifying compounds which modulate a proliferative disorder (e.g. tumor establishment, tumor growth, tumor metastasis, epithelial cell proliferation, endothelial cell proliferation, neuronal cell growth, and wound healing) which occur in a broad range of types of cells and tissues. These effects occur *in vitro*, in cells in culture, and *in vivo*, in a whole organism, with a broad range of physiological effects.

The evaluation of the ability of the test compound to modulate this broad range of effects in a broad genus of cell and tissue types is based purely on the binding of the compound to a broad scope of polypeptides, which is largely undefined biologically or structurally, without any evaluation of the effect of binding of the compound on the target polypeptide, and whether any activity on the polypeptide is effected, and how that would further relate to the modulation of any of the specifically claimed proliferative disorders. The specification fails to provide guidance for the degree of binding or the specificity or strength of binding sufficient to produce

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any meaningful physiological outcome related to the specifically claimed proliferative disorders. Further, the claims are so broad as to encompass methods wherein the binding of a compound to a fragment of a polypeptide is assessed, whether or not the fragment has any relevance physiologically, for example, whether the fragment used in the assay folds to resemble the protein as it would occur in a cell and, therefore, whether the fragment has any possible meaning in relation to the specifically claimed proliferative disorders. As claimed, the methods assess mere binding of compounds that bind to a polypeptide, however, simple binding would not provide any reliable information regarding a compound's ability to modulate any of the physiological effects the claimed methods are directed to. Further, the specification has not provided any guidance to enable the skilled artisan to extend the determination of binding in the claims to any meaningful information to determine if the candidate compound modulates the broad range of proliferative disorders claimed. Simple determination of binding would not predictably translate into an ability of a compound to modulate any of the broad range of proliferative disorders, as claimed. Further, the specification discloses one particular preferred embodiment of the polypeptide used in the claimed methods, SEQ ID NO:2, but it is unclear whether SEQ ID NO: 2, or a polypeptide 95% identical to SEQ ID NO:2, or a polypeptide fragment of 400 amino acids of SEQ ID NO:2, has any effect on the claimed proliferative disorders in a cell. The specification discloses that SEQ ID NO:2 is only a predicted polypeptide sequence encoded by nucleic acid sequences which are expressed differentially when cells were grown in soft agar versus plastic (see Example 5). The expression of these nucleic acids also appeared to be high in many normal tissue types, diseased tissues and in xenograft cell lines (see Table 5 and 6 and Results Summary page 95). The results of expression profiling of the nucleic

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acids encoding SEQ ID NO:2, discussed on pages 101-102, indicate there is variability in expression levels among different tumor tissues and normal tissue types. The variable nature of the expression indicates that although nucleic acids encoding SEQ ID NO:2 may be differentially expressed in some tissue types and some cancer tissues, it is unclear how these expression levels correlate with any particular physiological conditions. Further, a differential level of expression of these nucleic acids would not predictably correlate with the modulation of any of the specifically claimed proliferative disorders, as assessed in the claimed methods. For example, it is unclear that the expression levels of these nucleic acids is involved in the regulation of any proliferative disorder, or, for example, a response to a disease condition. For example, if the differential expression is a response to a disease state, binding a compound to the polypeptide product, even if it modulates activity of the polypeptide, would not modulate the proliferative disorder claimed. The specification has given no guidance on the actual activity of the polypeptide encoded by these nucleic acids (SEQ ID NO:2), except to speculate that the protein is a novel sulfatase based on sequence similarity with other potential sulfatases, and its relation to the specifically claimed phenomena is based on speculation that other members of the sulfatase family may be involved in these proliferative disorders. The level of guidance provided by the specification about the specifically claimed polypeptide is scant and the skilled artisan would not predictably expect to determine compounds that modulate the broad range of physiological phenomena as claimed based on mere binding since the function of SEQ ID NO:2 in relation to proliferative disorders remains to be determined. To practice the claimed methods, the skilled artisan would need to undergo undue trial and error experimentation, beyond the teachings and guidance of the specification, to determine compounds bind SEQ ID NO:2 to

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modulate the broad range of proliferative disorders claimed, for the broad range of tissue and cell types encompassed in the claims. Even through such undue trial and error experimentation, it is unpredictable that the skilled artisan would ever be able to determine such compounds, since it is unclear that SEQ ID NO:2 is even involved in any relevant way to the specified proliferative disorders or if that binding to SEQ ID NO:2 would provide any information on a candidate compounds ability to modulate such proliferative disorders.

Response to Arguments

It is noted that in the previous Office Action mailed November 18, 2003, claims 28-30 were rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. It is noted that the Amendment filed April 1, 2004, canceled claims 28-30. However, in light of the presenting pending claims, the Examiner will address Applicants arguments.

Applicant's arguments have been fully considered, but are not found persuasive. Applicants argue that the specification enables one of skill in the art to carry out the invention using fully characterized 95% variants of SEQ ID NO:2, having sulfatase activity, and fragments of at least 400 contiguous amino acids of SEQ ID NO:2, having sulfatase activity, without undue experimentation. This is not found persuasive because as discussed above, the specification provides no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to amino acid changes and substitutions and the nature and extent of changes that can be made in these positions in order to obtain protein that exhibits the functionality of the claims.

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Applicants argue that the specification teaches that compounds, or candidate compounds, such as, for example, small molecules and peptides, can be screened using various types of assays in order to identify compounds which bind to or modulate the activity of the polypeptide of the invention or a fragment thereof. This is not found persuasive because as discussed above, the claims encompass methods wherein any type of compound is tested for binding to a broad range of variant polypeptides and polypeptide fragments, a major portion of which have not been described, and therefore, also not characterized by the instant specification (see also 35 U.S.C. 112, first paragraph rejection for written description above).

Applicants argue that the steps recited in the claims would enable one of skill in the art to identify candidate compounds for modulating a proliferative disorder. This is not found persuasive because as discussed above, as claimed, the methods assess mere binding of compounds that bind to a polypeptide, however, simple binding would not provide any reliable information regarding a compound's ability to modulate any of the physiological effects the claimed methods are directed to. Further, the specification has not provided any guidance to enable the skilled artisan to extend the determination of binding to provide any meaningful information to determine if a compound modulates the range of proliferative disorders claimed, as simple determination of binding would not predictably translate into an ability of a compound to modulate any proliferative disorder, as claimed. Applicants disagree with the Examiner's assertion that a differential level of expression of these nucleic acids would not predictably correlate with the modulation of any of the specifically claimed phenomena as an increase in expression of a polypeptide of the invention in a diseased tissue or cell as compared to the level of expression of the polypeptide under normal physiological conditions is indicative that the

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polypeptide is either involved in the regulation of the disease phenomena or is responding to the disease state. This is not found persuasive because the specification has not given any guidance on the actual activity of the polypeptide encoded by these nucleic acids (SEQ ID NO:2), or their biological role in proliferative disorders except to speculate that the protein is a putative novel sulfatase, based solely on sequence similarity with other potential sulfatases. Further Applicants allege that the relation of SEQ ID NO:2 and the claimed proliferative disorders is based on speculation that other members of the sulfatase family may be involved in these disorders.

The level of guidance provided by the specification about the specifically claimed polypeptides is scant and the skilled artisan would not predictably expect to determine compounds that modulate the broad range of proliferative disorders from the claimed method. Applicants contend that if one of skill in the art is able to identify candidate compounds which have been selected based on their ability to bind to a polypeptide, such candidate compounds may be capable of modulating a proliferative disorder by either 1) increasing the polypeptide's activity (which may be useful if the polypeptide is responding to the disease state); or 2) decreasing the polypeptide's activity (which may be useful if the polypeptide is involved in the regulation of the proliferative disorder). This is not found persuasive because it is unclear the polypeptide of the invention (SEQ ID NO:2) is even biologically involved in any kind of proliferative disorder, or if determination of binding to SEQ ID NO:2 would provide any information on a compounds ability to modulate such disorders.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg

September 16, 2004



JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600